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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/085,484	02/26/2002	Luminita Pricop	5983/OK209	4903

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EXAMINER	
MAHATAN, CHANNING	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/085,484	PRICOP, LUMINITA	
	Examiner	Art Unit	
	Channing S. Mahatan	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *10-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1 Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

APPLICANTS' ELECTION

Applicant's election of Group I (claims 1-9; drawn to a method for assessing susceptibility of systemic lupus erythematosus) in the reply filed on 19 January 2005 is acknowledged. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)).

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 1-9. Claims 10-21 are withdrawn from consideration as directed to a non-elected invention.

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

SCOPE OF ENABLEMENT

Claims 1, 2, 3, and 5-8 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for "an FcγRIIB promoter gene" wherein the polymorphic positions within are at residue positions –385 (C/C genotype) alone and in combination with –119 (T/A or A/A genotype), does not reasonably provide enablement for "at least one polymorphic position within an FcγRIIB promoter gene" as broadly encompassed by the instant claims.

Factors to be considered in determining whether a disclosure would require undue

experimentation have been summarized in Ex parte Forman, 230 U.S.P.Q. 546 (B.P.A.I. 1986) and reiterated by the Court of Appeals in In re Wands, 8 U.S.P.Q. 2d 1400 at 1404 (C.A.F.C. 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The specification discloses the following regarding "an FcγRIIB promoter gene" the specification indicates the following:

> "Figure 1 shows the nucleotide sequence of the 5' promoter region of human FcγRIIB gene (SEQ ID NO: 1)." (page 6, lines 24-25)
>
> "A 536 bp region of the 5' untranslated region (5' UTR) (SEQ ID NO: 1) of the human FcγRIIB gene in over 300 donors was sequenced." (page 29, lines 9-10)
>
> "The presence of the (-385 G/C) heterozygous genotype and the -385 homozygous C/C genotype was confirmed by sequencing 164 Caucasian SLE patients and 102 Caucasian non-SLE controls. The -385C/C genotype was present in 7.9% of SLE patients vs 0.98% Caucasian non-SLE controls, and was significantly (P=0.034) higher in SLE patients than in healthy adults. Table 1 shows the distribution of alleles of the FcγRIIB promoter in SLE patients and healthy controls. The odds ratio for -385 C/C homozygous individuals to develop SLE was 8.7 compared to those who were not -385 C/C homozygous (-385 G/C or -385 G/G), p=0.02 (two sided Fisher's exact test), 95% confidence interval on odds ratio 1.3-373. The actual number of alleles in normal individuals (182G and 22C) compared to individuals with lupus (278G and 50C) was not significantly different (p=0.183).
> In the process of sequencing the proximal promoter region of the human FcγRIIB gene in reverse direction, a second SNP (T to A) was identified, at position -119 relative to the start of the first exon (or position -77 from the transcription initiation site). The homozygous -119 A/A genotype was identified in four donors, who were also homozygous C/C at the -385 locus, three of which had SLE. The heterozygous -119 T/A genotype was identified in 3 additional SLE donors and 2 normal controls.

> The results suggest that C is associated with A in both lupus ($p<0.001$) and normals ($p=0.02$), and that C/C differs from the G carrying group in the T-A distribution." (pages 30-31, beginning on line 14)

However, the instant claims are not specifically limited to SEQ ID NO: 1 and polymorphic positions –385 and –119 (as recited above). In view of such deficiency the instant claims broadly encompass other potential unidentified polymorphic positions within "an FcγRIIB promoter gene" that would require one of skill in the art to perform further undue experimentation. For example, one of skill in the art would be required to first isolate "an FcγRIIB promoter gene", systematically (via tests and validations) identify polymorphic positions therein (nucleotide by nucleotide), such that the comparison of these positions within a "test polymorphic pattern..." and a "reference polymorphic pattern..." provides for the conclusion that an individual is or is not susceptible to development of systemic lupus erythematosus. Applicant is directed to Fields, Wilkinson, and Kende v. Conover and Woodward [170 USPQ 276; How-to-Make Requirement section] which states:

> "the description must place the invention in the possession of the public as fully as if the art or instrument itself had been practically and publicly employed. In order to accomplish this, it must be so particular and definite that from it alone, without experiment or the exertion of his own inventive skill, any person versed in the art to which it appertains could construct and use it."

Such independent decisions, judgments, tests, and validation are not considered to be routine experimentation and one of skill in the art practicing the invention would be required to use inventive skill to develop protocols for the automated classification of chromatograms and the validation of such classification therein. The instantly claimed invention broadly embraces polymorphic positions within an FcγRIIB promoter gene beyond that which is taught and/or described by the specification. Thus, the specification provides limited guidance for the limitation "at least one polymorphic position within an FcγRIIB promoter gene" utilized in the

instantly claimed invention. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

VAGUE AND INDEFINITE

Claims 1 and all claims dependent therefrom recite in the preamble "A method for assessing susceptibility of systemic lupus erythematosus in an individual to be tested comprising comparing..." and the final step of "concluding whether the individual is susceptible to development of systemic lupus erythematosus" which is considered vague and indefinite. It is understood that "a test polymorphic pattern" and "a reference polymorphic pattern" are to be compared to one another, it is unclear what the criteria/parameters (as broadly encompassed) are for said comparison such that a conclusion is drawn on whether the individual is susceptible to development of systemic lupus erythematosus. While the specification does provide the following regarding the disclosed invention:

> "The invention provides methods for assessing whether a particular individual has a genetic predisposition to systemic lupus erythematosus (SLE). This aspect of the invention comprises comparing a test polymorphic pattern established by a polymorphic position within a gene encoding the FcγIIB receptor (FcγRIIB) with a polymorphic pattern of individuals having SLE. The assessment depends on whether the individual's polymorphism pattern matches the reference pattern." (page 5, lines 14-19)

> "The method of the invention is carried out by comparing a test polymorphic pattern established by a polymorphic position within a gene encoding the FcγRIIB with a polymorphic pattern of a population of individuals having SLE (reference pattern). If the test pattern matches the reference pattern, there is a statistically significant probability that the individual has or may develop SLE." (page 5, lines 23-27)

The instant claims do not recite the limitation that such criteria/parameter for the conclusion is that the "test pattern" matches the "reference pattern" as provided for in the above cited portion of the specification. In such absence the instant claims are interpreted to broadly encompass an unclear & unlimited number of criteria/parameters for the conclusion that an individual is susceptible to development of systemic lupus erythematosus. Clarification of the metes and bounds, via clearer claim language, is requested.

Claims Rejected Under 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kimberly et al. (U.S. Patent Number 5,830,652) further in view of Jiang et al. (Genetically determined aberrant down-regulation of FcγRIIB1 in germinal center B cells associated with hyper-IgG and IgG autoantibodies in murine systemic lupus erythematosus. International Immunology. June 1999, Volume 11, Number 10, pages 1685-1691).

Kimberly et al. describes a method for determining whether the Fcγ (i.e. FcγRIIA) receptor allelic pattern of the patient (i.e. test pattern) corresponds most closely to known Fcγ receptor allelic patterns (i.e. polymorphic pattern) of patients having autoimmune disease (i.e.

reference pattern of patients), such that one can determine if an individual has a predisposition (i.e. susceptibility) for systemic lupus erythematosus (instant claims 1, 2, and 8; Abstract; Column 3, lines 3-11; Column 4, lines 22-25 & 33-40; and Example 4). However, Kimberly et al. does not utilize "at least one" or "at least two" "polymorphic positions within an FcγRIIB promoter gene".

Jiang et al. describes the identification of polymorphisms within the FcγRIIB promoter gene, which can be utilized to determine the predisposition of an individual for systemic lupus erythematosus". (Abstract; page 1686, left column, lines 42-46; page 1686-1687 "Genotyping" section; and page 1688, left column, lines 23-38; and Table 3).

Therefore, one of ordinary skill in the art at the time of the invention would have combined the diagnostic method for determining predisposition to systemic lupus erythematosus in a patient of Kimberly et al. with the polymorphisms identified in the FcγRIIB promoter taught by Jiang et al., since Jiang et al. indicates that the FcγRIIB promoter polymorphisms may possibly predispose to systemic lupus erythematosus (Abstract; page 1690, right column, lines 10-11). Further, Kimberly et al. provides that the disclosed method can be applied to systemic lupus erythematosus (Column 4, lines 33-35).

EXAMINER COMMENT

With respect to "polymorphic pattern" the specification provides the following:

> "A "polymorphism pattern" as used herein denotes a set of one or more polymorphisms, including without limitation single nucleotide polymorphisms, which may be contained in the sequence of a single gene or a plurality of genes. In the simplest case, a polymorphism pattern can consist of a single nucleotide polymorphism in only one position of one of two alleles of an individual. However, one has to look at both copies of a gene. A "test polymorphism pattern" as used herein is a polymorphism pattern determined for a human subject of undefined SLE status. A "reference polymorphism pattern" as used herein is determined from a statistically significant correlation of patterns in a population of individuals having SLE." (page 9, lines 13-21)

OBJECTION TO DISCLOSURE

The disclosure is objected to because of the following informalities:

The specification contains a typographical error on page 36, line 20; wherein "by Real time PCR" should be replaced with "by real time PCR". Appropriate correction is requested.

The use of the trademark throughout this application has been noted (pages 19, 27, 29, 30, 34, 35, and 36. It should be capitalized wherever it appears and be accompanied by the generic terminology. For example, page 19, lines 2-3 recite the trademark names Novagen and Invitrogen which are not capitalized and do not have proper trademark designation. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Appropriate correction is requested.

INFORMATION DISCLOSURE STATEMENT

It appears Applicants have submitted an '*INFORMATION DISCLOSURE STATEMENT*', which was filed 07 January 2005. However, absent is PTO-1449 Form. It should be noted that the citation "PCT/US03/04111" has been considered.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either 571-273-8300.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify Applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables Applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Examiner Initials: CSM

Date: March 29, 2005

ARDIN H. MARSCHEL 3/29/05
PRIMARY EXAMINER